



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Pasternak et al. Confirmation No. 3048
U.S. Serial No. 09/806,645 Examiner: Wang, Shengjun
Filed: July 12, 2001 Group Art Unit: 1617
For: TOPICAL COMPOSITION COMPRISING AN OPIOID ANALGESIC
AND AN NMDA RECEPTOR ANTAGONIST

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CERTIFICATION UNDER 37 C.F.R. §1.10

Date of Deposit: November 16, 2006

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Deborah Clark
Name of Person Mailing Paper


Signature of Person Mailing Paper

DECLARATION OF GAVRIL W. PASTERNAK, M.D. PH.D

I, Gavril W. Pasternak, declare as follows:

1. I hold the position of Attending Neurologist and Head of the Laboratory of Molecular Neuropharmacology at Memorial Sloan-Kettering Cancer Center. I also hold the position of Professor of Neurology & Neuroscience, Pharmacology and Psychiatry at the Weill College of Medicine of Cornell University. I am an inventor of U.S. Patent Application No. 09/806,645 ("the present application"). I am familiar with the present application and its filing. My curriculum vitae is attached under Tab A. I respectfully submit that I am qualified to speak and render opinions as to the disclosure in the present application and the state of the

Attorney Docket No. 51590.62072 US

art, as I am considered an expert in the field and have familiarity with the present application and its prosecution.

2. I am familiar with the Office Action dated January 18, 2006, and the Advisory Action dated May 5, 2005, both issued by the United States Patent and Trademark Office in connection with the present application and make this Declaration in response thereto. I understand that the Examiner questions whether one of ordinary skill in the art could extrapolate the data generated using the tail-flick assay in the present application to "any topical area of any mammal" particularly a human.
3. I hold the opinion that one of ordinary skill in the art would be able to extrapolate the data generated using the tail-flick assay in the present application to the topical area of a mammal, particularly a human.
4. The tail-flick assay described in the present application has been in use by those of skill in the art since about 1943.
5. The tail-flick assay was chosen to evaluate the invention of the present application because the neuroanatomy and neurophysiology of the skin innervating the tail of both rats and mice closely mimics that of human skin.
6. In the tail-flick assay, nociceptive stimuli is administered to the tail of the rodent which elicits a neurophysiological response.
7. The neurophysiological response generated by the tail-flick assay is predictive of the response in other mammals, including humans.
8. As of July 16, 1998, the tail-flick assay was validated as a predictor for analgesic activity in humans for a wide range of analgesic agents.

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9. As of July 16, 1998, the tail-flick assay was accepted by those of skill in the art for its reliability in predicting clinical outcome of opioid analgesics, morphine and morphinomimetic compounds in other mammals, including humans.
10. I understand that the Examiner also questions whether the description on page 20, lines 1-10 and lines 23-25, of the specification suitably describes a method in which the active agents of the invention (e.g., ketamine and morphine) are delivered to local peripheral receptors and not to central receptors. This passage describes certain results relating to the tail immersion technique. Briefly, it was determined that proximal segments of the tail which were not exposed to an opioid solution were not analgesic, confirming the peripheral site of action for the sites immersed in the opioid solution. This finding confirmed the distribution studies with ¹²⁵I-opioid, which documented the localization of the radiolabel only to the regions immersed in drug solution and the absence of any significant uptake into the blood or the central nervous system. One skilled in the art would instantly recognize that this passage describes a method in which the active agents of the invention are effectively delivered to local peripheral receptors and not to central receptors.

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11. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements

Dated 15 November 2006

By: 

Gavril W. Pasternak, MD PhD

Anne Burnett Tandy Chair in Neurology
Member and Attending Neurologist
Head, Laboratory of Molecular
Neuropharmacology
Memorial Sloan-Kettering Cancer Center

Professor of Neurology & Neuroscience,
Pharmacology and Psychiatry
Weill College of Medicine of Cornell
University

Tel: 646 888-2165

Fax: 646 422-0271

Curriculum Vitae **Gavril W. Pasternak, M.D., Ph.D.**

Date/Place of Birth 29 June 1947; Brooklyn, N.Y.
Nationality United States of America

Professional Address Memorial Sloan-Kettering Cancer Center **Tel** (646) 888-2165
 1275 York Avenue **Fax** (646) 422-0271
 New York, NY 10021 **e mail:** pasterng@mskcc.org

Home Address 500 East 83rd Street, Apt 21M
 New York, NY 10021

Licensed Physician Maryland 1977 (Inactive)
 New York 1979

Board Certification Neurology, American Board of Psychiatry and Neurology 1980

Education Johns Hopkins University (Baltimore, Maryland),
 1969, B.A. Chemistry
 Johns Hopkins University School of Medicine,
 1973, M.D.
 1975, Ph.D. Pharmacology and Experimental Therapeutics

Postdoctoral Training Johns Hopkins School of Medicine
 1974-75, Fellow, Pharmacology and Experimental Therapeutics
 Johns Hopkins Hospital
 1975-76, Intern in Medicine
 1976-78, Assistant Resident, Resident, Fellow in Neurology

Current Appointments

Memorial Sloan-Kettering Cancer Center
 Member (1989-present)
 Anne Burnett Tandy Chair of Neurology (2005-present)

Memorial Hospital
 Attending Neurologist, Dept. of Neurology (1989-present)
 Attending Physician, Pain Service, Dept of Neurology (1989-present)

Sloan-Kettering Institute
 Member (1989-present)
 Head, Laboratory of Molecular Neuropharmacology

Weill Medical School of Cornell University
 Professor of Neurology and Neuroscience (1989-present)
 Professor of Pharmacology (1989-present)
 Professor of Psychiatry (1998 present)

Weill Graduate School of Medical Sciences of Cornell University
 Professor of Neurology and Neuroscience (1989-present)
 Professor of Pharmacology (1989-present)
 Professor of Molecular Pharmacology and Therapeutics (1990-present)
 Co-Director, Summer Minority Science Program (1994-2003)

The New York Hospital
 Attending Neurologist (1989-present)

Previous Appointments

Memorial Sloan-Kettering Cancer Center

Associate Member (1984-1989)

Memorial Hospital

Assistant Attending Neurologist, Dept of Neurology (1979-1985)

Assistant Attending Physician, Pain Service, Dept Neurology (1979-1985)

Associate Attending Neurologist, Dept of Neurology (1985-1989)

Associate Attending Physician, Pain Service, Dept Neurology (1985-1989)

Sloan-Kettering Institute for Cancer Research

Research Associate (1979-1984)

Associate Member (1988-1989)

Cornell University Medical College

Assistant Professor of Neurology (1979-1983)

Assistant Professor of Pharmacology (1979-1984)

Associate Professor of Neurology (1983-1989)

Associate Professor of Pharmacology (1984-1989)

Cornell University Graduate School of Medical Sciences

Director (1989-1992)/Co-Director (1992-1997),

Graduate Program of Neuroscience

The New York Hospital

Assistant Attending Neurologist (1979-1983)

Associate Attending Neurologist (1983-1989)

Professional Societies

American Neurological Association

American Academy of Neurology, Fellow

American Society for Pharmacology & Experimental Therapeutics

College of Problems of Drug Dependence

American Association for the Advancement of Science

International Association for the Study of Pain

American Pain Society

Eastern Pain Association

New York Academy of Sciences

Phi Beta Kappa

Sigma Xi Scientific Society

Society for Neuroscience

The Harvey Society

Honors

2006	1 st Annual Machaskee Memorial Lectureship, Cleveland Clinic Cleveland, OH
2002-06	Listed, "Best Doctors in America", by Best Doctors, Inc.
2005	Anne Burnett Tandy Chair in Neurology, MSKCC
2004-09	Senior Scientist Award, National Institute on Drug Abuse
2002	The Millennium Prize 2002 and Lecture, by the Faculty of Medicine, Norwegian University of Science and Technology
2002	Listed, "Highly Cited Researchers", by ISI/Thomson Scientific (Original Member)
2001	US Lacrosse (Men's Division Coaches Council, Secondary Schools Metro Division): Man of the Year
2001	The John J. Bonica Award of the Eastern Pain Association.
1999-04	Senior Scientist Award, National Institute on Drug Abuse
1997	Wellcome Visiting Professor in the Basic Medical Sciences, U. of South Florida
1996	MERIT Award, National Institute on Drug Abuse (DA07242)
1994-99	Research Scientist Award, National Institute on Drug Abuse
1993	Elected to the Johns Hopkins University Society of Scholars
1990	Visiting Professor, Department of Anesthesiology, U. of California, San Diego
1990	Visiting Professor, Departments of Anesthesiology and Neuroscience, U. Cincinnati Med Center
1989	Sally Harrington Goldwater Memorial Visiting Professor, Barrow Neurological Institute
1989	Research Scientist Development Award, National Institute on Drug Abuse
1988	Lilly Clinical Scholar and Visiting Professor
1987-92	Board of Scientific Counselors, National Institute on Drug Abuse
1987	Tenth Annual Eino Nelson Memorial Conference Lecturer
1987	Louise and Allston Boyer Young Investigator Award for Clinical Investigation, Memorial Sloan-Kettering Cancer Center
1987	Visiting Professor, Department of Neurology, Loyola U. Stritch School of Medicine
1986	Visiting Professor, Department of Neurology, New Jersey Medical School
1984	Fellow, American Academy of Neurology
1984	Granito Memorial Lecture, New Jersey Pharmaceutical Association
1983	Visiting Professor, Department of Neurology, Tufts New England Medical Center
1980	S. Weir Mitchell Award of the American Academy of Neurology
1979-84	Teacher-Investigator Award (NINCDS)
1974	Drug Abuse Center Fellowship Award
1971	Insurance Medical Scientist Scholarship Award
1969	Phi Beta Kappa
1968	Phi Lambda Upsilon, Honorary Chemical Society
1968	Alpha Epsilon Delta, Honorary Premedical Society
1965	Bausch & Lomb Science Award

Editorial Responsibilities**Journals**

J. Pharmacology & Experimental Therapeutics.	Editorial Advisory Board, (1988-)
Molecular Pharmacology.	Editorial Board (1998-)
Brain Research	Editorial Board (2002-2006)
	Board of Reviewing Editors (2006-)
Life Sciences.	Editorial Advisory Board (1984-)
Cellular and Molecular Neurobiology.	Editorial Board (1987-)
Synapse.	Editorial Board (1994-)
Analgesia Reviews (previously Analgesia)	Editorial Board (1994-)
Neuroscience-Net.	Editorial Board (1996-)
Palliative Medicine	Editorial Advisory Board (2002-)
Neuropharmacology	Executive Editor (1998-);
	Editorial Board (1987-1992)
BioTechniques	Editorial Board (1990- 1996)
Receptors and Signal Transduction	Editorial Board (1989-1998)
The Pain Clinic Journal.	Editorial Board (1988-1998)
PharmacologyOnLine	Editorial Board (2006-)
Faculty of 1000	Editorial Board (2006-)

Books: Analgesics: Neurochemical, Behavioral and Clinical Perspectives

M.J. Kuhar and G.W. Pasternak, editors, Raven Press, New York, 1984.

The Opiate Receptors, G.W. Pasternak, editor, Humana Press, New York, 1988.

Patents

- #4,608,376: Opiate agonists and antagonists
- #4,803,208: Opiate agonists and antagonists
- #5,747,279: Nucleic acid molecules encoding kappa₃ receptors, receptors encoded thereby, and uses thereof
- #6,509,028: Methods and compositions for treating pain of mucous membrane
- #6,500,927: Identification and characterization of multiple splice variants of the mu-opioid receptor gene
- #6,627,734: Identification and characterization of multiple splice variants of the kappa₃-related opioid receptor (KOR-3) gene
- #6,660,496: Nucleic acid molecules encoding a KOR3 kappa opioid receptor and the methods of producing the encoded receptor
- #6,790,855: Topical anesthetic/opioid formulations and uses thereof
- #6,825,203: Topical anesthetic/opioid formulations and uses thereof
- #7,087,714: Mu-Opioid receptor splice variant polypeptides

Extramural Activities

National Institute on Drug Abuse
 Board of Scientific Counselors (1987-1992)
 Molecular, Cellular and Chemical Neurobiology Study Section
 Chairman (1994-1996)
 Member (1992-1996)

National Institutes of Health
 Molecular, Developmental and Cellular Neuroscience (MDCN5) Study Section
 Member (1999- 2003)
 Ad Hoc Reviewer (1996-1999; 2003-present)

American Academy of Neurology
 Auxiliary Awards Committee (1994-1998)

American Association Advancement of Science; Medical Sciences Section (1990-1994)

New York Academy of Sciences; Conference Committee (1988-1994)

Johns Hopkins University
 National Alumni Schools Committee (1990-present)
 Alumni Council (1998-2001)

External Advisory Committee, Specialized Neuroscience Research Program,
 Hunter College (2001-present)

Farber Institute for the Neurosciences of Thomas Jefferson University
 Member, External Scientific Advisory Board (2003 present)

EpiCept Corporation (Englewood Cliffs, NJ)
 Member and Chairman, Scientific Advisory Board (1999- present)

Syntem Corporation (Nimes, France)
 Member, Scientific Advisory Board (2000- 2006)

Director-At-Large, Eastern Pain Association (2002- 2004)

Limerick NeuroSciences Inc.
 Member, Scientific Advisory Board (2006 present)

Intramural Activities

Memorial Hospital
 Institutional Review Board (1983-1987; 1989-1995)
 Credentials Committee (1993-2004); Chairman (1999- 2004)
 Memorial Hospital Committee on Credentials, Appointments and Promotions (MHCCAP)
 Co-Chair (2004-present)
 Member, Memorial Hospital Medical Board (1999-2005)
 Member, MSKCC Committee on Appointments and Promotions (1999-present)
 Research Council (1997-2001)

Sloan-Kettering Institute
 Executive Committee, Program of Molecular Pharmacology and Chemistry
 (1989-present)
 Chairman, Institutional Animal Care and Use Committee (IACUC) (1999-present)

Cornell U. Medical College/New York Hospital
 Executive Committee, Department of Neurology (1992-1997)
 M.D.-Ph.D. Program
 Executive Committee (1993-1996)
 Admissions Committee (1996-1999)

Cornell U. Graduate School of Medical Sciences
 Director (1989-1992)/Co-Director (1992-1997), Program in Neuroscience
 Faculty Advisory Committee (1989-1997); Vice-Chair (1996-1997)
 Executive Advisory Committee (1996-1997)
 Curriculum Committee, Program in Neuroscience (1989-1992)
 Credentials Committee, Program in Neuroscience (1989-1995)
 Admissions Committee, Program in Neuroscience (1989-1997)

Marital Status: Sandra F. Pasternak (deceased)

Dependents
Katie Rachael Pasternak
David Avram Pasternak
Anna Rose Pasternak

I. Published Papers

1. PASTERNAK GW. Differentiation and characterization of opiate agonist and antagonist binding. Doctoral Dissertation, Johns Hopkins University, Baltimore, Maryland, 1974.
2. COWAN DO, PASTERNAK GW and KAUFMAN F. Biological electron transport systems. *Proc. Nat. Acad. Sci. USA*, 66: 837-843, 1970.
3. HARIK SI, PASTERNAK GW and SNYDER SH. An enzymatic isotopic microassay for putrescine. *Biochem. Biophys. Acta*, 304: 753-764, 1973.
4. PERT CB, PASTERNAK GW and SNYDER SH. Opiate agonists and antagonists discriminated by receptor binding in brain. *Science*, 182: 1359-1361, 1973.
5. HARIK SI, PASTERNAK GW and SNYDER SH. Putrescine: a sensitive assay and blockade of its synthesis by hydrazino-ornithine. In Polyamines in Normal and Neoplastic Growth D.H. Russell (Ed.). New York, Raven Press, 1973, p. 307-321.
6. PASTERNAK GW and SNYDER SH. Opiate receptor binding: effects of enzymatic treatments. *Mol. Pharmacol.* 10: 183-193, 1974.
7. PASTERNAK GW and SNYDER SH. The effect of enzymatic treatments on ³H-Naloxone binding. *Proc. Comm. Drug Dependence*, 370-375, 1974.
8. PERT CB, PASTERNAK GW and SNYDER SH. Opiate agonists and antagonists discriminated by receptor binding in brain. *Proc. Comm. Drug Dependence* p. 376-382, 1974.
9. SNYDER SH, PERT CB and PASTERNAK GW. The opiate receptor. *Ann. Int. Med.* 81: 534-540, 1974.
10. PASTERNAK GW and SNYDER SH. Identification of novel high affinity opiate receptor binding in rat brain. *Nature*, 253: 563-565, 1975.
11. PASTERNAK GW, GOODMAN R and SNYDER SH. An endogenous morphine-like factor. In The Opiate Narcotics: Neurochemical Mechanisms in Analgesia and Dependence. A. Goldstein (Ed.), New York, Pergamon Press, 1975, p. 13-17.
12. CREESE I, PASTERNAK GW, PERT CB and SNYDER SH. Discrimination by temperature of opiate agonist and antagonist receptor binding. In The Opiate Narcotics: Neurochemical Mechanisms in Analgesia and Dependence. A. Goldstein (Ed.), New York, Pergamon Press, 1975, p. 85-90.
13. SNYDER SH, PASTERNAK GW and PERT CB. Opiate receptor mechanisms. In Handbook of Psychopharmacology, Vol. 5, L. Iversen, S. Iversen and S.H. Snyder (Eds.). New York, Plenum Press, 1975, p. 329-360.
14. SNYDER SH, PERT CB and PASTERNAK GW. Opiate receptor dynamics. In Proceedings of the IX Congress of the Collegium Internationale Neuropsychopharmacologicum, Paris, 7-12 July 1974, J.R. Boissier, H. Hippius and P. Pichot (Eds.). Amsterdam, Excerpta Medica 1975, p. 307-313.
15. GUARNIERI M, KRELL LS, MCKHANN GM, PASTERNAK GW and YAMAMURA HI. The effects of cell isolation techniques on neuronal membrane receptors. *Brain Res.*, 93: 337-342, 1975.
16. WILSON HA, PASTERNAK GW and SNYDER SH. Differentiation of opiate agonist and antagonist receptor binding by protein modifying reagents. *Nature* 253: 448-450, 1975.

17. TELL GP, PASTERNAK GW and CUATRECASAS P. Brain and caudate nucleus adenylate cyclase: effects of dopamine, GTP, E prostaglandins and morphine. *FEBS Letters*, 51: 242-245, 1975.
18. MARCH SC, PASTERNAK GW, PARIKH I, SNYDER SH and CUATRECASAS P. Macromolecular Naloxone: a long-acting opiate antagonist. *Proc. Comm. Drug Dependence*, p. 607-611, 1975.
19. PASTERNAK GW and SNYDER SH. An endogenous morphine-like factor in mammalian brain. *Proc. Comm. Drug Dependence*, p. 460-470.
20. PASTERNAK GW, SNOWMAN AM and SNYDER SH. Selective enhancement of [3 H]-opiate agonist binding by divalent cations. *Mol. Pharmacol.*, 11: 735-744, 1975.
21. PASTERNAK GW, GOODMAN R and SNYDER SH. An endogenous morphine like factor in mammalian brain. *Life Sci.*, 16: 1765-1769, 1975.
22. PASTERNAK GW, WILSON HA and SNYDER SH. Differential effects of protein modifying reagents on receptor binding of opiate agonist and antagonists. *Mol. Pharmacol.*, 11: 348-351, 1975.
23. PASTERNAK GW and SNYDER SH. Opiate receptor binding: enzymatic treatments discriminate between agonist and antagonist interactions. *Mol. Pharmacol.* 11: 478-484, 1975.
24. CREESE I, PASTERNAK GW, PERT CB and SNYDER SH. Discrimination by temperature of opiate agonist and antagonist receptor binding. *Life Sci.* 16: 1837-1842, 1975.
25. PASTERNAK GW, SIMANTOV R and SNYDER SH. Characterization of an endogenous morphine-like factor (enkephalin) in mammalian brain. *Mol. Pharmacol.* 12: 504-513, 1976.
26. PASTERNAK GW, MARCH S, PARIKH I, SNYDER SH and CUATRECASAS P. Macromolecular naloxone: a novel class of long-acting polymer drugs. *Life Sci.*, 18: 977-982, 1976.
27. SIMANTOV R, KUCHAR M, PASTERNAK GW and SNYDER SH. The regional distribution of a morphine-like factor, "enkephalin," in monkey brain. *Brain Res.*, 106: 189-197, 1976.
28. SNYDER SH, SIMANTOV R and PASTERNAK GW. The brain's own morphine, "endorphin": a peptide neurotransmitter? *Neurosci. Symp.*, 1: 82-98, 1976.
29. PASTERNAK GW, SIMANTOV R and SNYDER SH. An endogenous morphine-like factor. In Tissue Responses to Addictive Drugs, Ford and Clouet (Eds.). New York, Spectrum Publications, 1976, p. 103-122.
30. RAWLINGS W, BYNUM TE and PASTERNAK GW. Pancreatic ascites: diagnosis of leakage site by endoscopic pancreatography. *Surgery*, 81: 363-365, 1977.
31. SNYDER SH, CHILDERS SR and PASTERNAK GW. Opiate receptors: A) functional heterogeneity demonstrated with an apparently irreversible naloxone derivative; B) regulation by guanine nucleotides. In Advances in Pharmacology and Therapeutics, Vol. 1: Receptors. J. Jacob (Ed.). New York, Pergamon Press, 1978, p. 39-46.
32. ARABI BA, PASTERNAK GW, HURKO O and LONG DM. Familial intradural arachnoid cysts. *J. Neurosurg.*, 50: 826-829, 1979.
33. PASTERNAK GW, CHILDERS SR and SNYDER SH. Multiple opiate receptors: evidence for mediation of analgesia by a subpopulation of receptors. In Endogenous and Exogenous Opioid Agonists and Antagonists, E.L. Way (Ed.) New York, Pergamon Press, 1979, p. 113-116.

34. PASTERNAK GW, CHILDERS SR and SNYDER SH: Opiate analgesia: evidence for mediation by a subpopulation of opiate receptors. *Science*, 208: 514-516, 1980.
35. CORREA FMA, INNIS RB, ROUOT B, PASTERNAK GW and SNYDER SH. Fluorescent probes of α - and β -adrenergic and opiate receptors: biochemical and histochemical evaluation. *Neurosci. Letters*, 16: 433, 1980.
36. PASTERNAK GW and HAHN EF. Long-acting opiate agonists and antagonists: 14hydroxydihydromorphinone hydrazones. *J. Med. Chem.*, 23: 674-677, 1980.
37. PASTERNAK GW. Multiple opiate receptors: ^3H -ethylketocyclazocine receptor binding and ketocyclazocine analgesia. *Proc. Nat. Acad. Sci. USA*, 77: 3691-3694, 1980.
38. PASTERNAK GW, ZHANG A-Z and TECOTT L. Developmental differences between high and low affinity opiate binding sites: their relationship to analgesia and respiratory depression. *Life Sci.*, 27: 1183-1190, 1980.
39. PASTERNAK GW, CHILDERS SR and SNYDER SH. Naloxazone, a long-acting opiate antagonist: effect on analgesia in intact animals and on opiate receptor binding in vitro. *J. Pharmacol. Exp. Therap.* 214: 455-462, 1980.
40. ZHANG A-Z and PASTERNAK GW. Mu and delta opiate receptors: correlation with high and low affinity opiate binding sites. *Europ. J. Pharmacol.* 67: 323-324, 1980.
41. PASTERNAK GW. Endogenous opioid systems in brain. *Amer. J. Med.* 68: 1571-159, 1980.
42. HAZUM E, CHANG KJ, CUATRECASAS P and PASTERNAK GW. Naloxazone irreversibility inhibits the high affinity binding of [^{24}I]D-al 2 -D-leu 5 -enkephalin. *Life Sci.*, 28: 2973-2979, 1981.
43. ZHANG A-Z and PASTERNAK GW. Opiates and enkephalins: a common binding site mediates their analgesic actions in rats. *Life Sci.*, 29: 843-851, 1981.
44. ZHANG A-Z, CHANG J and PASTERNAK GW. The actions of naloxazone on the binding and analgesic properties of morphiceptin (NH $_2$ -Tyr-Pro-Phe-Pro-CONH $_2$), a selective mu-receptor ligand. *Life Sci.*, 28: 2829-2836, 1981.
45. BUATTI MC and PASTERNAK GW. Multiple opiate receptors: phylogenetic differences. *Brain Res.*, 218: 400-405, 1981.
46. ZHANG A-Z and PASTERNAK GW. Ontogeny of opioid pharmacology and receptors: high and low affinity site differences. *Europ. J. Pharmacol.*, 73: 29-40, 1981.
47. PASTERNAK GW. Opiate, enkephalin and endorphin analgesia: relations to a single subpopulation of opiate receptors. *Neurology*, 31: 1311-1315, 1981.
48. PASTERNAK GW, CARROLL-BUATTI M and SPIEGEL K. The binding and analgesic properties of a sigma opiate, SKF 10,047. *J. Pharmacol. Exp. Therap.*, 219: 192-198, 1981.
49. PASTERNAK GW. The neuropharmacology of pain. *Urban Health*, 10: 32-33, 48, 1981.
50. WOLOZIN BL and PASTERNAK GW. Classification of multiple morphine and enkephalin binding sites in the central nervous system. *Proc. Nat. Acad. Sci. USA*, 78: 6181-6185, 1981.
51. PASTERNAK GW. Central mechanisms of opioid analgesia. *Acupuncture and ElectroTher.*, 6: 135-149, 1981.
52. HAHN EF, CARROLL-BUATTI M and PASTERNAK GW. Irreversible opiate agonists and antagonists: the 14

hydroxydihydromorphinone azines. *J. Neurosci.*, 2: 572-576, 1982.

53. SPIEGEL K, KOURIDES I and PASTERNAK GW. Prolactin and growth hormone release by morphine in the rat: different receptor mechanisms. *Science* 217: 745747, 1982.
54. CHILDERS SR and PASTERNAK GW. Naloxazone, a novel opiate antagonist: irreversible blockade of rat brain opiate receptors in vitro. *Cell. Molec. Neurobiol.*, 2: 93103, 1982.
55. WOLOZIN BL, NISHIMURA S and PASTERNAK GW. The binding of kappa and sigma opiates in rat brain. *J. Neurosci.*, 2: 708-713, 1982.
56. GALETTA S, LING GSF, WOLFIN L and PASTERNAK GW. Receptor binding and analgesic properties of oxymorphone. *Life Sci.*, 31: 1389-1392, 1982.
57. JOHNSON N, HOUGHTEN R and PASTERNAK GW. Binding of ^3H - β -endorphin in rat brain. *Life Sci.*, 31: 1381-1384, 1982.
58. PASTERNAK GW. High and low affinity opioid binding sites relationship to mu and delta sites. *Life Sci.* 31: 1303-1306, 1982.
59. HAHN EF and PASTERNAK GW. Naloxonazine, a potent, longacting inhibitor of opiate binding sites. *Life Sci.* 31: 1385-1388, 1982.
60. NISHIMURA S and PASTERNAK GW. Opiate and opioid peptide binding in rat and goldfish: further evidence for opiate receptor heterogeneity. *Brain Res.*, 248: 192195, 1982.
61. PASTERNAK GW and CHILDERS SR. Opiate and opioid peptide actions in the central nervous system. In Recent Advances in Clinical Pharmacology (P. Turner and D.G. Shand, Eds.), Churchill-Livingston Press, p. 253-279.
62. SPIEGEL K, KOURIDES IA and PASTERNAK GW. Different receptors mediate morphine-induced prolactin and growth hormone release. *Life Sci.* 31:21772180, 1982.
63. LING GSF and PASTERNAK GW. Morphine catalepsy in the rat: involvement of μ (high affinity) opioid binding sites. *Neurosci. Letters.* 32:193-196, 1982.
64. BURKHARDT C, FREDERICKSON RC and PASTERNAK GW. Metkephamid (Tyr-D-ala-gly-phe-N(Me)MetONH₂), a potent opioid peptide: receptor binding and analgesic properties. *Peptides.* 3:869-871, 1982.
65. PASTERNAK GW. Psychotropic drugs and chronic pain. In Diagnosis and Treatment of Chronic Pain (N. Hendler, D. Long and T. Wise, Eds.) Wright PSG Press. pp 201-210.
66. KIRCHGESSNER AL, BODNER RJ and PASTERNAK GW. Naloxazone and pain-inhibitory systems: evidence for a collateral inhibition model. *Pharmacol. Biochem. Behav.* 17:11751179, 1982.
67. SPIEGEL K, KALB P and PASTERNAK GW. Analgesic activity of tricyclic antidepressants. *Annals Neurol.* 13:462-465, 1983.
68. LING GSF, SPIEGEL K, NISHIMURA S and PASTERNAK GW. Dissociation of morphine's analgesic and respiratory depressant actions. *Eur. J. Pharmacol.* 86:487-488, 1983.
69. PASTERNAK GW. New approaches to chronic pain. *Drug Therapy*, May, 1983. p. 128.
70. WOOD PL and PASTERNAK GW. Specific μ_2 opioid isoreceptor regulation of nigrostriatal neurons: in vivo

evidence with naloxonazine. *Neurosci. Lett.* 37:291-293, 1983.

71. LING GSF and PASTERNAK GW. Spinal and supraspinal analgesia in the mouse: the role of subpopulations of opioid binding sites. *Brain Res.* 271:152-156, 1983.
72. HOLADAY JW, PASTERNAK GW, D'AMATO RJ, RUVIO BA and FADEN AI. Naloxazone lacks therapeutic effects in endotoxic shock yet blocks the effects of naloxone. *Eur. J. Pharmacol.* 89:293-296, 1983.
73. JOHNSON N and PASTERNAK GW. The binding to rat brain homogenates of Mr2034; A universal opiate. *Life Sci.* 33:985-991, 1983.
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